



EV 317349164 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

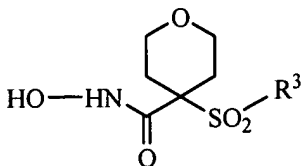
Application of: Barta et al.
Serial No: 09/311,837
Filed: May 14, 1999
Title: Aromatic Sulfone Hydroxamic Acid Metalloprotease Inhibitor
Confirmation No: 1791
Group Art Unit: 1625
Examiner: Celia Chang
Attorney Ref: 3124/4/US (formerly 116.6/US)
HDP Ref: 6794-000021/US

Supplemental Declaration of Joseph J. McDonald

I, Dr. Joseph J. McDonald, declare the following:

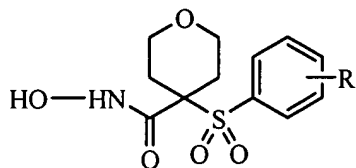
1. I am a named inventor in the above-referenced patent application.
2. I am a group leader in computational chemistry at Pfizer, Inc. I was a group leader in computational chemistry at Pharmacia Corporation, the assignee of the above-referenced patent application.
3. My statement in Paragraph 5 of my November 2, 2001 declaration needs clarification. Specifically, that paragraph should be revised in the following manner:

The above table shows MMP inhibition data for tetrahydropyranyl compounds having a single-ring **phenyl** substituent on the sulfonyl, **wherein the phenyl is the only ring structure in the substituent**. The compounds in the above table are the only such compounds that I could locate in the Pharmacia database at my disposal where the compound corresponds in structure **to** the following formula with R³ being the substituent on the sulfonyl:





4. After further searches of the Pharmacia compound database at my disposal, I have identified additional tetrahydropyranyl compounds synthesized and/or tested by Pharmacia and having the following formula, wherein R does not contain a ring structure:



Those compounds, and their corresponding MMP-1 and MMP-13 inhibition data, are shown in the following table:

Tetrahydropyranyl Compounds with a Single-Ring Phenyl Substituent on the Sulfonyl

Compound	MMP-1 Inhibition K_i (IC_{50})	MMP-13 Inhibition K_i (IC_{50})
	1210	21
	>10000	393
	5950	8.82
	3880	8.47
	2190	3.82



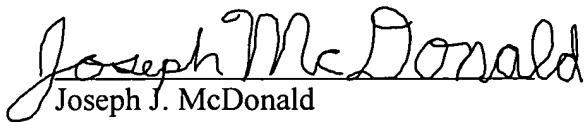
Compound	MMP-1 Inhibition K_i (IC_{50})	MMP-13 Inhibition K_i (IC_{50})
	2410	1.36
	3720	1.09
	>10000	3.68
	>10000	2360
	2110 3720	0.99 6.59
	>10000	35.7
	2540	0.467
		(22.4)



Compound	MMP-1 Inhibition K_i (IC_{50})	MMP-13 Inhibition K_i (IC_{50})
		(25)
	>10000	(230)
	>10000	(2.1)
	(>10000)	(1300)
		(1.8)
	5720	721
	(1800)	(48.5)

5. The MMP inhibition data in the above table was obtained by the methods generally described, for example, in the above-referenced patent application and U.S. Patent No. 6,689,794. All IC_{50} and K_i values are presented in nM.

6. All statements made in this declaration of my own knowledge are true and all statements made on information and belief are believed to be true; and further, these statements have been made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under 18 U.S.C. §1001, and that such willful, false statements may jeopardize the validity of the above-referenced patent application or any patent issuing thereon.


Joseph J. McDonald

May 20, 2004 _____
Date